REMARKS/ARGUMENTS

Upon entry of the instant amendment, claims 92-124 are pending in the instant application. Claims 1-91 have been canceled without prejudice. Claims 92-124 are new. Applicants respectfully submit that the new claims do not introduce new matter and are made without any intention to abandon the subject matter as filed, but with the intention that claims of the same, greater, or lesser scope may be filed in a continuing application.

The applicant maintains the right to file a divisional application that will include the subject matter of claims 1-91 that are now canceled.

EXAMINER INTERVIEW

Applicant thanks Examiner Oh and Supervisor Michael G. Hartley for the meeting with Applicant's agent, D'vorah Graeser (Registration number 40,000), on October 31, 2006 in which the rejections of the claims in the Office Action of July 3, 2006 were discussed.

Rejections Under 35 U.S.C. §102(b)

The Examiner rejected claims 48-91 under 35 U.S.C. 103(a) as being unpatentable over Heese et al. (U.S. Patent No. 6,623,759) in view of Bergstrand et al. (U.S. Patent No 5,817,338). Applicant respectfully traverses the rejections.

The Examiner states that the composition described in the Heese et al. patent discloses a core coated with a polymer layer that is resistant to gastric acid, that is neutralized to a range of pH 5.5 to 7.0, and therefore has the functional properties of an enteric coating layer. In the view of the Examiner, such a characterization reads on limitations set forth in the instant claims, such that this polymer layer is not merely an intermediate layer. The Examiner further states that there is no additional layer that exists between the neutralized enteric layer and the core, and that although Heese et al. teaches the presence of an additional layer over the neutralized layer, the open scope of the claim

language of the present application does not forbid the inclusion of additional outer coating layers over the neutralized enteric coating layer.

New claims 92-94 as presented herein are directed towards methods of production of tablet compositions, in which a single, neutralized enteric layer is applied directly to a substrate, without the use of an intermediate layer. The term 'consisting essentially of', has been used with regard to the method steps in order to emphasize the limitation of having only these steps being performed, which overcomes rejections related to the language being too broad by virtue of being open.

In contrast to the invention of the instant application, Heese et al. teach a neutralized polymer layer, which has the functional properties of an enteric layer, which is then coated with second enteric coating, as an outer layer, which is a customary enteric, gastric juice resistant layer (column 6, lines 5-9). The prior art neither teaches nor suggests a formulation for a benzimidazole having a core and a single, neutralized enteric layer, with no additional enteric coating layers. The possibility of providing a stable formulation for the benzimidazole which does not require the use of an additional, outer enteric coating layer is neither taught nor suggested by Heese et al.

The method of Bergstrand et al. involves the formation of many pellets, each comprising a substrate which is separately coated with enteric coating, then compressed into a tablet. In contrast, the methods of the present invention consist essentially of formation of a single substrate which features the benzimidazole derivative, onto which is coated a single enteric coating layer, thereby forming the tablet, with no compression step after application of the enteric layer.

The combined disclosures of Heese et al. and Bergstrand et al. do not teach a method for producing a stable benzimidazole formulation, involving applying a single, neutralized, enteric coating layer directly to a substrate.

The Examiner has rejected claims 40-47 under 35 U.S.C. 103(a) as being unpatentable over Scheiwe et al. (U.S. Patent No. 6,149,942). The Examiner states that Scheiwe et al. teach a pharmaceutical pellet formulation of omeprazole, comprising a core containing the active agent. An enteric lacquer is then applied over the core. This coating layer can further comprise optional components such as pH adjusting agents, which include strong bases such as sodium hydroxide, as well as buffering agents.

In the view of the Examiner, the broad disclosure of the prior art makes the instantly claimed invention obvious. The Examiner considers that despite the absence of an explicit disclosure of a neutral or basic pH of the enteric coating, one of ordinary skill in the art would be able to reasonably expect that an enteric coating layer comprising a sufficiently strong alkaline agent would have a neutral or basic pH.

Scheiwe et al. teaches a pharmaceutical formulation with a core containing omeprazole as the active ingredient, in which the storage stability is greatly improved by the addition of TiO_2 to the core, and optionally to the enteric coating. The use of other adjuncts, such as pH correctors, is taught as being optional, and is clearly not the focus of the invention.

Furthermore, Scheiwe does not teach or suggest the importance of *neutralized* enteric coating. It is possible to add such pH adjusting agents to an enteric coating without neutralizing it; by contrast, Applicant's invention requires such neutralization. The language concerning the basic pH has been removed from the current claims to further clarify that neutralization is an important component of the present invention.

Although one skilled in the art may suppose that an enteric coating layer comprising a sufficiently alkaline agent might possibly alter the pH of the coating layer, it would not be obvious that neutralization is required (as opposed to a mere alteration of the pH), nor would it be obvious that the use of such a neutralized coating layer would

obviate the requirement for a separating layer between the omeprazole-containing substrate and the enteric coating layer in the absence of titanium dioxide.

Hence it is clear that no indication is provided in the patent of Scheiwe et al. that stability may be achieved by the use of a neutralized enteric coating. Instead, Scheiwe et al. teach that the use of TiO_2 is required for stability. In contrast, the present invention does not require the use of TiO_2 in order to provide a stable formulation, as shown in Example 2, wherein titanium dioxide is omitted. Stability tests carried out on the formulation of Example 2, as described in Example 7, demonstrated excellent stability of the formulation.

It is therefore clear that none of the cited references teaches or suggests a method which includes the preparation of *neutralized* enteric coating, nor does any cited reference teach or suggest the ability of such a neutralized enteric coating to provide a stabilized formulation without a subcoating layer. The cited references certainly do not teach or suggest a method limited to the above steps.

As per the request of the Examiners during the Interview, Applicant has agreed to also indicate at least some of the many differences between the present invention as currently claimed and previously cited art, without concurring with any indication of relevancy of such references to the present invention as claimed and also without crafting a rejection thereto.

Reference WO 99/27917 to Dietrich et al., cited under 35 U.S.C. 102(b) in the Office Action of April 23, 2003, teaches a preparation in the form of a pellet or tablet for acid-labile active substances, comprising an alkaline core and a gastric juice-resistant coating comprising a neutralized film former. The method taught by Dietrich involves separate application of a film polymer having neutralized carboxyl groups, and of a second layer comprising a dispersion of non-neutralized stomach acid resistant polymer film former, which is also sprayed on. The steps of applying at least two enteric coating

layers, including at least one non-neutralized layer, are therefore taught by Dietrich, in contrast to the application of a single neutralized enteric layer as recited in the currently presented claims.

The Office Action of April 23, 2003 further cited Dietrich et al. in view of Lundberg et al. (U.S. Patent No. 6,013,281) and Lee et al. (U.S. Patent No. 6,228,400 B1), under 35 U.S.C. 103(a).

Lundberg teaches an oral pharmaceutical dosage form comprising an alkaline reacting core material and an enteric coating layer, such that a separating layer is formed in situ as a water soluble salt between the alkaline core material and the enteric coating polymer. The step of neutralizing a solution of an enteric coating polymer prior to applying the solution to a substrate is neither taught nor suggested by Lundberg.

Lee teaches a formulation comprising a subcoat between the core and the enteric coating. A method involving the application of a neutralized enteric coating directly to the substrate, without the use of an intermediate layer, is not taught.

Therefore, the combination of Dietrich and Lundberg clearly does not teach or suggest the present invention, nor does the combination of Dietrich, Lundberg and Lee, nor indeed does any combination of any references described herein teach or suggest the present invention.

The present response is intended to be fully responsive to all points of objection raised by the Examiner and is believed to place claims 92-104 in condition for allowance. Favorable reconsideration and allowance of the Application is respectfully requested.

NEW CLAIMS

New independent claim 92 is based on previous claim 83, with the added limitations that the enteric coating material is selected from a specified group of polymers, as supported by the specification at page 7, last paragraph; and that the alkalizing material may be an inorganic or organic alkaline compound, as supported by the specification at page 4, last paragraph.

New independent claim 103 is based on previous claim 83, with the further limitations that the enteric coating material is selected from the group of polymers defined above for claim 92, in the form of an aqueous solution, as supported by the specification at page 5, lines 24-26; that the alkalizing material is one of sodium, potassium or ammonium hydroxide, as taught on page 4, line 32, bridging page 5, line 1; and that the enteric solution is applied by spraying, as taught in Examples 1-4.

New independent claim 114 is based on previous claim 83, with the further limitations that the enteric coating material is an aqueous solution of a polymer selected from the group defined for claim 103, with the added limitation that the alkalizing agent is ammonium hydroxide, as supported by the specification at page on page 4, line 32, bridging page 5, line 1; and that a plasticizer is added to the solution, as supported by the specification at page 5, second paragraph.

New dependent claims 93-95, 104-106, and 115-117 recite that the neutralized solution of claims 92, 103, and 114, respectively, is at least 60%, 80% and 95% neutralized respectively, as taught in the specification at page 8, lines 5-7.

New dependent claims 96-99, 107-110, and 118-121, correspond to previous claims 84-87.

New dependent claims 100, 111, and 122 recite that the enteric coating is applied by spraying, and new claim 101, 112, and 123 specify the incoming air temperature at which the spraying is carried out, as supported by Examples 1-4 which teach the incoming air temperature as being at least 40°C.

New dependent claims 103, 113, and 124 recite that the solution may be applied by pan coating or fluidized bed coating, as supported by the specification at page 8, lines 10-12.

CONCLUSION

Applicant believes that the claims are in condition for allowance. If the Examiner believes that a telephonic interview with the undersigned would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned at (301) 952-1011.

Respectfully submitted,

Date: January 2, 2007
Reg. No. 40,000
Tel. No. (301) 952-1011

D'vorah Graeser, PhD
Agent for Applicant
c/o Discovery Dispatch
9003 Florin Way
Upper Marlboro, Maryland 20772

Attachment